

Please substitute the following CLAIM set for the pending claim set.

1. (Canceled)
2. (Canceled)
3. (Canceled)
4. (Canceled)
5. (Canceled)
6. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test

eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test
eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition
sites;

enumerating said sequence tags in the population to determine numbers of individual
sequence tags present in the population, wherein less than 100 % of the sequence tags calculated
to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second
number of copies of the plurality of sequence tags determined for a genome of a reference
eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence
tags are within a window of sequence tags which are calculated to be contiguous in the genome
of the reference eukaryotic cell, wherein the window spans about 40 kb, wherein a difference
between the first number and the second number indicates a karyotypic difference between the
test eukaryotic cell and the reference eukaryotic cell.

7. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 200 kb, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

8. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 600 kb, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

9. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome

of the reference eukaryotic cell, wherein the window spans about 4 Mb, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

10. (Canceled)

11. (Canceled)

12. (Canceled)

13. (Canceled)

14. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 15 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated~~in the step of enumerating;~~

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second

number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

15. (Canceled)

16. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, wherein the test eukaryotic cell is a cell of a person with a hereditary disorder, comprising:
generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;
enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;
comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

17. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, wherein the test eukaryotic cell is a cell of a person with an infectious disease, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

18. (Canceled)

19. (Original) ~~The method of claim 18~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by a first restriction endonuclease cleavage site at a first end of each portion and a second restriction endonuclease cleavage site at a second end of each portion, wherein the first restriction endonuclease is SacI;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

20. (Canceled)

21. (Original) ~~The method of claim 18~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by a first restriction endonuclease cleavage site at a first end of each portion and a second restriction endonuclease cleavage site at a second end of each portion, wherein recognition or cleavage by the first restriction endonuclease is sensitive to DNA methylation;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

22. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites, wherein said portions are defined by presence of a BcgI restriction endonuclease recognition site which is flanked by 12 nucleotides on either end;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second

number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

23. (Currently amended) ~~The method of claim 1~~ A method of karyotyping a genome of a test

eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine numbers of individual sequence tags present in the population, wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing a first number of copies of a plurality of sequence tags enumerated to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell; ~~further comprising:~~

identifying aneuploidy if (a) sequence tags of one or more autosomes are determined to be present in the test eukaryotic cell relative to the reference eukaryotic cell at a ratio of 1.5 or greater or less than 0.7; or (b) sequence tags of one or more sex chromosomes in a male are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at

a ratio of 1.5 or greater or less than 0.7; or (c) sequence tags of X chromosomes in a female are determined to be present in the test eukaryotic cell relative to a reference male eukaryotic cell at a ratio of 3 or greater or less than 1.5 or relative to a reference female eukaryotic cell at a ratio of 1.5 or greater or less than 0.7.

24. (Canceled)

25. (Cancelled)

26. (Cancelled)

27. (Cancelled)

28. (Cancelled)

29. (Cancelled)

30. (Cancelled)

31. (Cancelled)

32. (Cancelled)

33. (Cancelled)

34. (Cancelled)

35. (Cancelled)

36. (Cancelled)

37. (Canceled)

38. (Canceled)

39. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites, wherein said portions are defined by presence of a *BcgI* restriction endonuclease recognition site which is flanked by 12 nucleotides on either end;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

40. (Canceled)

41. (Canceled)

42. (Canceled)

43. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 40 kb, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

44. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in

the genome of the reference eukaryotic cell, wherein the window spans about 200 kb, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

45. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 600 kb, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

46. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 4 Mb, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

47. (Canceled)

48. ((Canceled)

49. (Canceled)

50. (Canceled)

51. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 15 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated in the step of enumerating;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

52. (Canceled)

53. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, wherein the test eukaryotic cell is a cell of a person with a hereditary disorder, comprising:
generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;
enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;
comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in

the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

54. (Currently amended) ~~The method of claim 37~~ A method of karyotyping a genome of a test eukaryotic cell, wherein the cell is a cell of a person with an infectious disease, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

55. (Currently amended) ~~The method of claim 38~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites, wherein said portions are defined by a first restriction endonuclease site at a first end of

each portion and a second restriction endonuclease site at a second end of each portion, wherein the first restriction endonuclease is *SacI*;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

56. (Canceled)

57. (Currently amended) ~~The method of claim 38~~ A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites, wherein said portions are defined by a first restriction endonuclease site at a first end of each portion and a second restriction endonuclease site at a second end of each portion, wherein recognition or cleavage by the first restriction endonuclease is sensitive to DNA methylation;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population wherein less than 100 % of the sequence tags calculated to be present in the genome of the eukaryotic cell are enumerated;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

58. -86. (Canceled)

87. (Previously Presented) A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating copies of said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population;

comparing the first number of copies of a plurality of sequence tags in the population to a second number of copies of the plurality of sequence tags determined for a genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 200 kb, wherein a

difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

88. (Canceled)

89. (Previously Presented) A method of karyotyping a genome of a test eukaryotic cell, comprising:

generating a population of sequence tags from defined portions of the genome of the test eukaryotic cell, said portions being defined by one or two restriction endonuclease recognition sites;

enumerating said sequence tags in the population to determine a first number of copies of a plurality of sequence tags present in the population;

comparing the first number of the plurality of copies of sequence tags in the population to a second number of copies of said plurality of sequence tags calculated to be present in the genome of a reference eukaryotic cell of the same species as the test eukaryotic cell, wherein the plurality of sequence tags are within a window of sequence tags which are calculated to be contiguous in the genome of the reference eukaryotic cell, wherein the window spans about 200 kb, wherein a difference between the first number and the second number indicates a karyotypic abnormality.

90. (Previously presented) A method of karyotyping a genome of a test eukaryotic cell, comprising:

identifying pieces of the genome of the test eukaryotic cell by determining nucleotide sequence of said pieces;

enumerating the pieces within a plurality of windows of fixed size of the genome,
wherein the window spans about 200 kb;

comparing a first number of pieces enumerated within a plurality of windows for the test eukaryotic cell to a second number of pieces enumerated within the plurality of windows for a reference eukaryotic cell, wherein a difference between the first number and the second number indicates a karyotypic difference between the test eukaryotic cell and the reference eukaryotic cell.

91. (Canceled)

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